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In the Supreme Court of the United States

OCTOBER TERM, 1972

No. 72-394

CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, ET AL., PETITIONERS

v.

HYNSON, WESTCOTT AND DUNNING, INCORPORATED

Nos. 72-414, 72-528, 72-555, 72-666

AND CONSOLIDATED CASES

ON WRIT OF CERTIORARI TO THE UNITED STATES COURTS OF APPEALS FOR THE THIRD AND FOURTH CIRCUITS

CONSOLIDATED REPLY BRIEF FOR THE FEDERAL PARTIES

Taken together, the industry briefs filed in these five cases would severely undermine the drug effectiveness provisions of the Act. The proposed impact of these industry briefs may be seen by examining collectively the following propositions for which they contend:

(1) In spite of the fact that the statutory standard for withdrawal of approval of an NDA, as with initial denial of approval, turns on the "lack" of sub-

stantial evidence of effectiveness (rather than requiring FDA to determine that the drug is in fact ineffective), once an NDA has been approved, the burden shifts to the agency to justify removal of the product from the market (although all the information relevant to the inquiry is in the possession of the manufacturer).[1]

(2) Even after the National Academy of Sciences-National Research Council, under contract with FDA, has found wholly inadequate support for the effectiveness of a drug, the FDA's own review has confirmed this evaluation, and neither the manufacturer nor any other interested person has identified substantial evidence of effectiveness, FDA must in some way come forward with additional information on its own before it may require the manufacturer to come forward with his evidence of effectiveness.[2]

(3) All that a manufacturer need do to obtain a hearing on withdrawal of an NDA is to make conclusory allegations sufficient, if proved, to present a factual issue, and FDA may not properly pierce those allegations to determine whether there is any basis whatever for them.[3]

(4) Withdrawal of NDA approval by FDA through the administrative process is largely academic anyway, because the manufacturer is thereafter free to relitigate basically indistinguishable issues *de novo* in

[1] Hynson Br., No. 72-394, pp. 39-41; PMA Br. 12-13; Squibb Br. 13-14.

[2] *Ibid.*

[3] Hynson Br., No. 72-394, pp. 42-43; PMA Br. 3-4, 22.

a district court in contending that the product is no longer a "new drug."[4]

(5) Even though the notice of proposed NDA withdrawal explicitly states that it applies to all me-too drugs, in fact all of those me-too drugs are free to ignore the administrative process and may thereafter relitigate all of the identical issues *de novo* in a district court.[5]

(6) In any event, the entire 1962 Amendments and the NDA withdrawal procedure apply only to the relatively few (no more than 4,000) products which shouldered the burden of complying with administrative regulatory procedures by obtaining an NDA during the 1938–1962 period, and not to the vast majority of the estimated 35,000 prescription and 100,000 to 500,000 OTC drugs now on the market.[6]

(7) Not only is the "no longer new drug" issue separable, to be relitigated *de novo* in district courts by every manufacturer, but all that need be shown to satisfy this exemption from the regulatory requirements of the Act is the very type of anecdotal opinion that Congress, after informed consideration, explicitly rejected as scientifically inadequate to demonstrate the effectiveness of drugs.[7]

(8) FDA is powerless to utilize any administrative procedure whatever, whether rulemaking, adjudication, or a combination of the two, to settle initially any issue of drug safety or effectiveness, except when

[4] CIBA Br. 6–14; PA Br. 73–75; PMA Br. 26–41.
[5] Bentex Br. 8–20; PA Br. 65–73, 75–77; PMA Br. 26–41.
[6] PA Br. 50–64; PMA Br. 41–54.
[7] Bentex Br. 6–7; PMA Br. 32–34.

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explicitly asked by the industry to do so in an individual case. It must resort directly to court enforcement in every instance rather than asserting its primary jurisdiction as the expert government agency on the safety and effectiveness of drugs.[8]

These briefs state that, whatever good intentions Congress might have had in enacting the 1938 Act and the 1962 Amendments, it simply failed to use sufficiently clear statutory language to effectuate its purposes, and therefore the matter must be referred back to Congress to repair the damage. Surely, Congress did not intend the narrow construction placed upon the Act or the constricted power attributed to FDA in these industry briefs. Both the statutory language and the legislative history make that clear. Nor can the industry advance any public policy for its proposed debilitation of the Act and of the agency's authority to implement it.

I. FDA Has Administrative Authority To Deal With a Broad Range of Drug Safety and Effectiveness Issues

At the heart of all five cases is the industry's attempt to limit FDA's authority to processing the specific NDAs which have been submitted to it and bringing lawsuits in the district courts to litigate the status of all other drugs. This approach would strip the agency of any real authority to accomplish the mandates laid down in the Act by Congress. Moreover, the powers attributed to FDA in the industry briefs

[8] PA Br. 21–49, 54–61; PMA Br. 34–41.

would be substantially smaller than those exercised by other administrative agencies. Since Congress has given broad and sweeping powers to many federal agencies dealing with purely economic matters, as this Court has recognized in numerous cases,[9] there is no reason why it would have intended to deny comparable authority to the agency entrusted with primary responsibility for protecting the health and safety of the nation with respect to drugs.

A. FDA HAS THE AUTHORITY TO DETERMINE, IN THE FIRST INSTANCE, ISSUES OF DRUG SAFETY AND EFFECTIVENESS

It is accepted practice that when dealing with problems whose dimensions go beyond a particular case and implicate an entire industry or major segments thereof, regulatory agencies are not required to operate on a narrow, case-by-case basis, but have authority to—and do—deal with them as broadly as necessary. The reason is obvious. Administrative agencies are created because of the need to apply expert knowledge and experience to particular segments of society or particular forms of conduct that have their own specialized problems and characteristics. The application of that expertise may indicate to the agency that a particular problem can be effectively solved only through comprehensive remedies. If, for example,

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[9] *E.g.*, *F.T.C.* v. *Colgate-Palmolive Co.*, 380 U.S. 374, 384–385 (F.T.C.); *United States* v. *Midwest Video Corp.*, 406 U.S. 649, 662–665 (F.C.C.); *American Power & Light Co.* v. *S.E.C.*, 329 U.S. 90, 112, and *S.E.C.* v. *Chenery Corp.*, 332 U.S. 194, 202–204 (S.E.C.); *N.L.R.B.* v. *Seven-Up Bottling Co.*, 344 U.S. 344, 346–347 (N.L.R.B.).

the public interest requires that a drug be removed from the market because it is unsafe or ineffective, the public would not be adequately protected if the only way FDA could do so would be by bringing 20 separate proceedings against each manufacturer of an example of the drug. The problem can properly be solved only by permitting FDA to act against the drug through a single proceeding in which each of the manufacturers involved could be heard.

This Court has recognized the authority of administrative agencies to deal with broad-scale problems on a broad enough basis for their effective solution. In *United States* v. *Storer Broadcasting Co.*, 351 U.S. 192, the Court upheld the rules of the Federal Communications Commission limiting the number of broadcasting stations a single individual may own as a proper exercise of the agency's "rule-making authority necessary for the orderly conduct of its business" (*id.* at 202). The Commission, of course, could have dealt with the problem of concentration of control in the broadcasting industry on a case-by-case basis. That is, instead of deciding that no individual could own more than five television stations, it could have determined appropriate limitations for each owner in separate proceedings concerning only that owner and the particular stations involved. This Court held, however, that its broad regulatory responsibilities authorized the agency to deal with the problem on a comprehensive basis.

FDA similarly is properly exercising its broad authority to protect the public from ineffective drugs by

dealing with the problem in the only practical way—through proceedings designed to prevent marketing of generic categories of drugs that do not satisfy the statutory standard. All manufacturers of each drug have full opportunity in these proceedings to show that the generic drug itself or their particular form of it is effective. There is no reason in fairness or precedent for requiring the agency to engage in protracted case-by-case district court litigation in which it would be required to prove the same thing over and over again, with respect to each manufacturer of what is essentially the same product.[10]

FDA has undertaken to implement the effectiveness requirements of the 1962 Amendments by two procedures designed to deal with these issues on a broad industry-wide basis. First, it has consistently taken the position—and has so advised the industry in every proceeding—that any withdrawal of NDA approval, (whether for a prescription or OTC drug) covers all me-too drugs.[11] Second, it has established administrative procedures to determine, in the first instance, the safety and effectiveness of OTC drugs,[12] and, depend-

[10] This Court stated in *S.E.C.* v. *Chenery Corp.*, 332 U.S. 194, 203, that "the choice between proceeding by general rule or by individual, *ad hoc* litigation is one that lies primarily in the informed discretion of the administrative agency."

[11] As in all the government briefs, a "me-too" drug includes all identical, similar, and related drugs, as defined at 37 Fed. Reg. 23185, which added Section 130.40 to 21 C.F.R.

[12] In the interest of fair play, FDA has proposed to defer implementation of the 1962 Amendments through withdrawal of NDA approval of over four hundred 1938–1962 OTC drugs until

ing upon the outcome of the present cases, intends to develop a similar procedure for settling the status of prescription drugs. These two approaches stand on basically the same legal footing—FDA's authority to engage in administrative regulation that comprises both adjudication and rulemaking. The industry briefs uniformly contend that both are unlawful and that FDA can decide these issues only with respect to those drugs for which an individual NDA has been filed with the agency for a specific drug product.[13]

In an NDA withdrawal proceeding, Section 5(e) of the Administrative Procedure Act, 5 U.S.C. 554(e), permits FDA to issue a declaratory order governing all drugs covered by that NDA. Section 701(a) of the Act broadly authorizes FDA "to promulgate regulations for the efficient enforcement of this Act," [14] subject of course to the notice-and-comment rulemaking procedure.

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after the comprehensive OTC drug review is completed. 37 Fed. Reg. 7807; see para. XV of the order entered in *American Public Health Assn.* v. *Veneman*, 349 F. Supp. 1311 (D.D.C.), 37 Fed. Reg. 26623, 26624. If FDA has no authority to determine the safety and effectiveness of OTC drugs through its current review procedures, 37 Fed. Reg. 85, 9464, the agency must proceed to withdraw those NDAs and to bring enforcement action against all me-too products.

[13] Br. for the Proprietary Association ("PA"), pp. 21–49, 54–61; PMA Br. 34–41.

[14] A similar broad authorization "to promulgate such rules and regulations as are necessary to carry out the provisions of this chapter" under the Poultry Products Inspection Act has been construed as "a general legislative power concerning matters covered by the Poultry Act *in addition* to whatever adjudicative power is conferred by particular provisions thereof." *Borden Co.* v. *Freeman*, 256 F. Supp. 592, 598 (D. N.J.). The PA Brief (pp. 39–41) and the PMA Brief (p. 29) argue that the provision for rulemaking after a "public hearing" in Section

PMA contends (Br. 35–36) that FDA has no authority to issue a declaratory order under the Administrative Procedure Act determining whether a drug is a "new drug" because that procedure is available to an agency only for "questions which it is otherwise authorized to adjudicate on the record of a hearing." The argument, of course, assumes the question at issue, *i.e.*, does FDA have authority in its administrative proceedings to determine whether a drug is a new drug? Section 5 of the Administrative Procedure Act, 5 U.S.C. 554, of which the provision authorizing declaratory orders is a part, primarily prescribes certain procedures that an agency must follow "in every case of adjudication required by statute to be determined on the record after opportunity for an agency hearing." Section 5(e), however, states that the agency "in its sound discretion, *may* issue a declaratory order to terminate a controversy or remove uncertainty" (emphasis added).

This provision *authorizes* an agency to issue declaratory orders in all cases of formal adjudication to which Section 5 applies, but it is not *limited* to that

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701(e) of the Act for certain specified types of regulations precludes use of the general rulemaking authority in Section 701(a) of the Act for other types of regulations. Congress has not required a public hearing for all FDA regulations, and FDA has in fact promulgated hundreds of substantive regulations under Section 701(a) which, as this Court has recognized, "have the status of law." *Abbott Laboratories* v. *Gardner*, 387 U.S. 136, 151–152. See also, *Pfizer, Inc.* v. *Richardson*, 434 F. 2d 536, 544 (C.A. 2), where Section 701(a) is characterized as granting "rule-making powers." Cf. *United States* v. *Allegheny-Ludlum Steel*, 406 U.S. 742, 757.

situation. Rather, it gives the agency broad discretion to issue a declaratory order whenever appropriate "to terminate a controversy or remove uncertainty." See *First Savings and Loan Association of the Bahamas, Ltd.* v. *Securities and Exchange Commission*, 358 F. 2d 358, 360 (C.A. 5), ruling that the Commission has authority under that provision to issue a declaratory order determining whether a foreign organization is exempt from the registration provisions of the Securities Act of 1933, even though the latter Act does not provide for adjudication on the record after opportunity for hearing of exemptions from its coverage. Similarly, FDA may issue a declaratory order to terminate a controversy or remove uncertainty over whether a particular drug is a "new drug" that is subject to the requirements of Section 505 of the Act.

In sum, therefore, in accordance with the admonition of the courts that "* * * agencies must exert the greatest resourceful, imaginative ingenuity in devising procedures which in a day of ever-expanding dockets will permit the regulatory process to function properly with reasonable dispatch," [15] it is well within the agency's authority to fashion administrative procedures designed to enforce the 1962 Amendments in the most direct and efficient manner consistent with fair play.

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[15] *F.T.C.* v. *J. Weingarten, Inc.*, 336 F.2d 687, 691–692 (C.A. 5). FDA's OTC drug review procedures have been regarded by one court as "calculated to achieve precisely the result applauded by the Fifth Circuit Court of Appeals in *Weingarten*," *United States* v. *Articles of Food and Drug* * * * *Coli-Trol 80 Medicated*, CCH Food, Drug, Cosmetic L. Rep., para. 40,837 (N.D. Ga.).

Indeed, even under the more primitive Food and Drug Act of 1906, this Court stated:

> Congress may declare its will, and, after fixing a primary standard, devolve upon administrative officers the "power to fill up the details" by prescribing administrative rules and regulatons. * * * [*United States* v. *Shreveport Grain & Elevator Co.*, 287 U.S. 77, 85.]

More specifically, in *Moog Industries, Inc.* v. *F.T.C.*, 355 U.S. 411, 413, this Court noted the responsibility of an administrative agency, in its discretion, "to develop that enforcement policy best calculated to achieve the ends contemplated by Congress," and in *F.T.C.* v. *Universal-Rundle Corp.*, 387 U.S. 244, 251, it admonished that such discretion does not include "unbridled power to institute proceedings which will arbitrarily destroy one of many law violators in an industry." [16] Yet in the instant cases the industry briefs argue that FDA *must* proceed on a case-by-case basis and is precluded from fashioning administrative adjudicatory and rulemaking procedures that will avoid the inequities that necessarily result from that approach.

B. MEANINGFUL DRUG EFFECTIVENESS REGULATION CANNOT BE ACCOMPLISHED BY DE NOVO CASE-BY-CASE LITIGATION

The industry briefs argue that litigation with respect to the safety and effectiveness of a drug, including the new drug status of a product, is a simple and

[16] See also *Columbia Broadcasting System* v. *United States*, 316 U.S. 407, 421.

straightforward matter, and thus entirely appropriate for the courts. In fact, however, such litigation is invariably protracted, it involves an enormous expenditure of government, industry, and court resources; it potentially includes so many products and issues that it would be impossible to make a substantial dent in the agency's task of removing ineffective drugs from the market by this means; it necessarily discriminates among competing products, because not all can be the subject of a court enforcement proceeding at one time; it promotes a lack of uniformity of results by having similar issues resolved by different courts; and in the end it fails to settle any issue because of the possibility of immediate product reformulation by the manufacturer, requiring new litigation.

The inadequacy of case-by-case judicial proceedings has been brought home forcefully by experience. FDA initially attempted through case-by-case litigation to apply the effectiveness requirements of the 1962 Amendments to products for which no NDA has been filed. It brought seizure actions against a few products [17] on the grounds that they were illegal new drugs marketed without an NDA and that they were misbranded. Just this handful of cases required a large expenditure of governmental manpower to prepare and present the necessary medical testimony. The typical case required obtaining affidavits or live testimony from between five and fifteen expert medical

[17] *E.g.*, Cetacaine Topical Anesthetic, Bentex Ulcerine, Chaser for Hangover, Mycocert, Mornin' Afta, Vice Spice, Xerac Alcohol Acne Gel, Asper-Sleep, Ornex, and Excedrin PM.

witnesses, often full professors or deans of medical schools. It became clear that FDA was incapable of a caseload of more than perhaps ten or fifteen such cases in any year, because of the heavy workload involved.

Moreover, this case-by-case approach is inherently unfair, because it requires compliance with the law by one manufacturer while his competitors remain free to violate it. Whether an NDA withdrawal proceeding or a court enforcement action is involved, FDA does not have the resources to institute the same action against all competing manufacturers of identical, similar, or related products unless all those products can be brought before the agency in an administrative proceeding at the same time.[18] In one recent instance involving court enforcement action brought by the agency, for example, the company argued that FDA had unfairly singled out its product. It pointed out (and FDA agreed) that there were at least 1200 competing products against which no action had been instituted.[19] The manufacturers of products whose NDAs have been withdrawn by the agency in the past three years have similarly complained bitterly to FDA that non-NDA'd me-too products still remain on the market.

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[18] See 37 Fed. Reg. 85–86.

[19] The product was seized by FDA. *United States* v. *An Article of Drug * * * Ornex Capsules*, No. 223–71 (D.N.J.). The company then brought an independent proceeding in a different court to enjoin FDA from taking further action against its product. *Smith Kline & French Laboratories* v. *Richardson*, No. 71–387 (E.D. Pa.).

Moreover, it rapidly became apparent that court enforcement actions frequently would settle little or nothing. In the *Xerac* case, for example, the government prevailed, after a protracted trial.[20] While the case was pending on appeal, however, the company's attorney informed FDA that it was reformulating the product. The issue then on appeal thus became largely academic, and FDA was faced with the choice of either beginning the litigation anew, with the realization that if it prevailed the company might again reformulate, or dropping the matter.[21]

FDA not only found such litigation costly, time-consuming, and unproductive, but increasingly found it difficult to obtain expert witnesses on the often trivial issues involved. It is not easy, for example, to obtain the time and services of a truly expert pharmacologist to testify that a fake aphrodisiac is in fact ineffective.[22]

On the other hand, the agency has been very successful in attracting the time and talent of the country's leading experts on drug safety and effectiveness in reviewing and developing broad standards for all products falling within a class, both in the completed NAS-NRC review and in the current re-

[20] *United States* v. * * * "*Xerac Alcohol Acne Gel*," CCH Food, Drug, Cosmetic L. Rep., para. 40,836 (N.D. Ill.).

[21] It is as a result of this experience that FDA elected to establish an administrative procedure (described in the government's *Bentex* brief, pp. 24–25) and has abandoned recourse to such useless litigation.

[22] *United States* v. *An Article of Drug* * * * *Vice Spice*, Civ. No. 35904 (E.D. Mich.).

views of OTC drugs, biologics, and diagnostic products. The major public benefits from such an approach are already being demonstrated in the OTC drug review.[22]

The industry briefs appear to take the position that FDA may impanel such experts to make determinations on safety and effectiveness, but that those determinations have no legal effect whatever. If those determinations could accomplish nothing more than to establish FDA's priorities for bringing enforcement

[22] The first proposed monograph for an OTC drug class of products, covering antacids, has recently been published. 38 Fed. Reg. 8714–8724. The manufacturers have already had an opportunity for a hearing before the expert panel that made the initial report, now have an opportunity for comment on the proposal, and will later have an opportunity for a further hearing before the Commissioner and for court review. 37 Fed. Reg. 85, 9464. The enormous amount of work that went into this proposal, and the potential benefit to the public as a result, are apparent on its face. If FDA were limited to implementing the NAS-NRC evaluations of the nineteen 1938–1962 NDAs that existed for OTC antacids (37 Fed. Reg. 7824–7827) and to bringing district court actions against unlawful drugs, as the Fourth Circuit held in *Bentex* and the industry briefs argue, and could not exercise primary jurisdiction over the subject matter to determine the issue initially through the administrative process (subject, of course, to judicial review), that notice and the entire OTC review procedure would be a nullity. The industry argues, indeed, that the only lawful purpose that can be attributed to such an administrative proceeding is to permit the agency to determine which lawsuits it will in fact file in the future. In short, each of the issues dealt with in this initial Federal Register notice for antacids would, in the event of substantial industry non-compliance, be required under this view to be relitigated *de novo* in district courts throughout the United States.

actions in the courts, however, the usefulness of such an administrative procedure—whether it involves withdrawal of an NDA for a drug (including all me-too versions) or determination of the safety and effectiveness of a class of drugs—would obviously be destroyed, and the doctrines of primary jurisdiction and exhaustion of administrative remedies would become meaningless in the field of drug regulation by the expert agency established for the purpose by Congress. While courts obviously must have the ultimate authority to determine the reasonableness of any rulemaking or adjudication undertaken by an administrative agency, the notion that such adjudication or rulemaking can do no more than assist the agency in establishing its court enforcement priorities undermines the ability of the agency to carry out its statutory responsibilities.

II. Hynson Was Not Improperly Denied a Hearing on Withdrawal of Lutrexin's NDA

The industry briefs, in discussing the issue raised by the government's petition in *Hynson* (No. 72–394), argue that a manufacturer is entitled to an evidentiary hearing on withdrawal of his NDA, as a matter of right, whenever he alleges the existence of adequate and well-controlled clinical studies, and that neither FDA nor a court may pierce those allegations to determine whether, on its face, the evidence proffered in fact may satisfy the requirements for an adequate and well-controlled clinical study as defined in the Commissioner's regulations. These briefs also urge,

on the basis of a recent decision of the District of Columbia Circuit, that FDA has the burden both to come forward with evidence to show a lack of effectiveness and to prove a lack of effectiveness before approval of an NDA may be withdrawn. They suggest that the lack of hearings to date and the fact that FDA is not an independent arbiter show the unfairness of the procedure followed by the agency. Finally, Hynson argues that it is entitled to a hearing because the FDA summary judgment regulations were adopted after it initially requested a hearing; it also contends that the evidence it presented is sufficient to justify a hearing if analyzed on the basis of "historical controls."

A. CONCLUSORY ALLEGATIONS THAT ADEQUATE, WELL-CONTROLLED STUDIES EXIST DO NOT SUFFICE TO REQUIRE A HEARING

Hynson argues flatly that Section 505 requires a hearing "if the applicant requests a hearing" (Br. 42).

The Pharmaceutical Manufacturers Association ("PMA"), although paying lip service to the proposition that no evidentiary hearing is required in the absence of a dispute over a material fact (Br. 11), empties the concept of significant meaning by asserting (Br. 20):

> Where the manufacturer offers the opinion of a qualified expert that a certain study or group of studies meets the criteria for an "adequate and well-controlled investigation" and establishes the effectiveness of a product, a genuine factual dispute is presented. That dispute can

> be resolved only through confrontation and cross-examination at an evidentiary hearing. * * *

Any manufacturer can allege—and, indeed, virtually always can find at least one physician to submit an affidavit in support of its contention—that adequate and well-controlled studies exist. If such an allegation suffices to require a hearing even though the studies, on their face, are clearly defective, hearings would, as a practical matter, be required on request.

Thus, the question is whether FDA is bound by the manufacturer's conclusory allegations in determining whether a hearing is appropriate, or whether it may look behind those allegations to determine whether the detailed requirements for an adequate and well-controlled clinical study set forth in the regulations are even possibly satisfied by any of the materials submitted to show effectiveness.

It is now well-established, in the judicial summary judgment context, that the trial judge is permitted, and indeed expected, to go behind the pleadings to determine whether an alleged issue of fact is real or imagined.[24] If the court deter-

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[24] *Kern* v. *Tri-State Insurance Co.*, 386 F.2d 754 (C.A. 8); *Robin Construction Co.* v. *United States*, 345 F.2d 610 (C.A. 3); *Perma Research & Development Co.* v. *Singer Co.*, 410 F.2d 572 (C.A. 2); *Bland* v. *Norfolk & Southern R.R. Co.*, 406 F.2d 863 (C.A. 4); *J. W. Scarboro, Jr.* v. *Universal C.I.T.*, 364 F.2d 10 (C.A. 5); *McKinney* v. *Armco Steel Corp.*, 270 F. Supp. 360 (W.D. Pa).

Rule 56 of the Federal Rules of Civil Procedure provides in pertinent part:

> **(e) Form of Affidavits; Further Testimony; Defense Required.** * * * When a motion for summary judgment is

mines, upon scrutiny of the affidavits, that the allegation is unsupportable and that there is actually no disputed material fact, summary judgment is of course permissible. This principle has been applied to FDA's summary judgment withdrawal proceedings in all cases except *Hynson. Upjohn Co.* v. *Finch,* 422 F.2d 944 (C.A. 6); *Pfizer, Inc.* v. *Richardson,* 434 F. 2d 536 (C.A. 2); *American Cyanamid* v. *Richardson,* 456 F. 2d 509 (C.A. 1); *Bristol Laboratories* v. *Richardson,* 456 F.2d 563 (C.A. 1); *Pharmaceutical Manufacturers Ass'n* v. *Richardson,* 318 F. Supp. 301 (D. Del.).

In the instant case, the conclusory assertions submitted by Hynson regarding the scientific adequacy of

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made and supported as provided in this rule, an adverse party may not rest upon the mere allegations or denials of his pleading, but his response, by affidavits or as otherwise provided in this rule, must set forth specific facts showing that there is a genuine issue for trial. If he does not so respond, summary judgment, if appropriate, shall be entered against him.

The "Notes of Advisory Committee on Rules," 28 U.S.C.A. following Rule 56, state as to this provision:

> The last two sentences are added to overcome a line of cases * * * which has impaired the utility of the summary judgment device. * * *
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> * * * * *
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> The very mission of the summary judgment procedure is to pierce the pleadings and to assess the proof in order to see whether there is a genuine need for trial. * * *
>
> * * * * *
>
> It is hoped that the amendment will contribute to the more effective utilization of the salutary device of summary judgment.

its studies do not overcome the plain fact that the studies themselves, on their face, fail in numerous respects to meet the criteria of the regulations. There is thus no basis for relying upon the face of the affidavits, as the Fourth Circuit did in this case, and ignoring the Commissioner's analysis of the defects in the underlying data submitted to support those affidavits.

B. IT IS ENTIRELY FAIR AND REASONABLE TO PLACE THE BURDEN ON THE NDA HOLDER TO COME FORWARD WITH A SHOWING THAT ADEQUATE STUDIES MAY EXIST

The industry briefs present a confusing description of the procedure used by FDA to withdraw NDA approval and are divided on the issue whether the *Hynson* case fully presents all of the issues inherent in that procedure. A review of the exact procedure used and the issues it presents to this Court is therefore appropriate.

In all of the cases now before this Court, the proceeding began with the receipt of an NAS–NRC evaluation of the drug in question. This evaluation was furnished to the manufacturer and was made known and furnished to all other manufacturers and to the public through a Federal Register notice, with a request for submission of any additional information that might establish the drug's effectiveness. On the basis of the information contained in the NDA file, any data submitted by the company to the NAS–NRC, the NAS–NRC report, and any additional information submitted by any person, the Commissioner

then made his own determination regarding withdrawal of the NDA, and if he decided tentatively that approval should be withdrawn, published an appropriate notice of opportunity for hearing in the Federal Register. The basis of this tentative determination was the conclusion of the NAS–NRC panels, showing a lack of substantial evidence of effectiveness, together with the absence of such a showing in any other materials then before the Commissioner.

The notice of opportunity for hearing provides thirty days within which the manufacturer or any other interested person may request a hearing. Under 21 C.F.R. 130.14(a) (J.A. 490), the manufacturer is entitled, upon request, to an explanation of the reasons for the Commissioner's proposed action. Hynson made no such request and cannot now complain, after failing to take advantage of this provision, that it should at that stage have received a fuller explanation of the Commissioner's reasons.

Under 21 C.F.R. 130.14(b) (J.A. 491), a request for a hearing must contain an organized, factual analysis identifying the existence of adequate and well-controlled clinical studies in order to show a genuine issue of fact on which the hearing might be held. In *Hynson,* a request for a hearing was made and the Commissioner carefully evaluated each of the scientific studies identified by Hynson to support effectiveness. The results of the Commissioner's evaluation, which showed that no adequate and well-controlled study was presented, were published in the Federal Register, and the hearing was denied. No

request for reconsideration of the Commissioner's determination was made.[25] The government believes that all aspects of this procedure are fully at issue in the *Hynson* case.[26]

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[25] If Hynson concluded that the Commissioner's evaluation was erroneous, it could have petitioned for reconsideration, and the Commissioner could then either "revoke" his order and "reinstate such approval" in accordance with Section 505(f) of the Act, or order a hearing, or take any other appropriate action justified by the petition. While the Commissioner's hearing regulations do not specifically provide for petitions for reconsideration, such petitions would be entertained. An administrative agency may, in its discretion, reopen any proceeding for reconsideration. *United States* v. *Pierce Auto Lines*, 327 U.S. 515, 534–535; *I.C.C.* v. *Jersey City*, 322 U.S. 503, 517–518; *Tagg Bros. & Moorhead* v. *United States*, 280 U.S. 420, 444–445; *American Chain & Cable Co.* v. *F.T.C.*, 142 F. 2d 909, 911 (C.A. 4); *Cia Mexicana De Gas* v. *F.P.C.*, 167 F. 2d 804, 806–807 (C.A. 5); *Sprague* v. *Woll*, 122 F. 2d 128, 130 (C.A. 7).

[26] In *USV Pharmaceutical Corp.* v. *Secretary of Health, Education, and Welfare*, 466 F. 2d 455 (C.A.D.C.), the order withdrawing approval of USV's bioflavonoid NDAs was reversed and the proceedings remanded, in part on the ground that the Commissioner had a burden to come forward with a statement of reasons supporting his proposed withdrawal and his notice of opportunity for hearing. In an *amicus* memorandum filed in the *Hynson* case (No. 72–394), USV contends that the issue of the burden of coming forward is not presented in *Hynson*. On the other hand, Hynson, PMA, and Squibb all rely heavily on such a contention in urging affirmance of the court of appeals' decision on the hearing issue. To the extent that Hynson, as a member of PMA, is free to assert this contention at all (see note 27, *infra*), we agree that it is properly in issue; if Hynson had the right to refuse to submit anything in response to the Commissioner's notice of opportunity for hearing, it should be no worse off simply because its submission was wholly inadequate.

Accordingly, if this Court determines that a hearing is not required in *Hynson*, and thus that the procedure followed

The industry briefs appear to take the position that FDA has the burden both to come forward with evidence showing a lack of the drug's effectiveness before it may propose to withdraw NDA approval and to prove the drug's ineffectiveness before denying a hearing on an NDA withdrawal. Neither of these positions is correct, and both positions have been specifically rejected in separate litigation brought by PMA (of which Hynson and USV are members). *Pharmaceutical Manufacturers Ass'n* v. *Richardson*, 318 F. Supp. 301, 312 (D. Del.).[27]

Under the 1962 Amendments, a drug manufacturer has the burden of showing the product's safety and effectiveness prior to marketing, and retains that burden throughout its marketing history. Sections 505 (d)(5) and 505(e)(3) of the Act both require NDA

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was lawful, FDA will provide USV another opportunity to submit data to justify a hearing, analyze any data so submitted to determine whether it indicates that adequate and well-controlled studies may exist, grant or deny a hearing in accordance with that determination, and, if it denies a hearing, publish its detailed analysis of the data in the Federal Register. If USV fails at that time to make a submission conforming to the requirements of the Commissioner's regulations, its request for a hearing will be summarily denied. The propriety of summary denial of a hearing in such circumstances was upheld in *Ciba-Geigy Corp.* v. *Richardson*, 446 F. 2d 466 (C.A. 2), which we believe adopts the correct view, and which conflicts in this regard with the opinion of the District of Columbia Circuit in the *USV* case.

[27] Since the propriety of FDA's procedures and procedural rules at issue here was adjudicated and the judicial determination was not appealed, the issues determined in the *PMA* litigation are *res judicata* as to PMA's members. See *Acree* v. *Air Line Pilots Association*, 390 F. 2d 199, 202 (C.A. 5).

disapproval or withdrawal of NDA approval not just if the drug is established by FDA to be unsafe or ineffective, but rather if at any time it is found that there is a lack of data to show safety and effectiveness. This approach places the burden of coming forward with data on the manufacturer, who is ordinarily the one who has developed the data in the first place. The statute places no different burden on FDA to disapprove the drug in the first instance than it does to withdraw approval later, since it uses the identical language in both provisions; nor does the legislative history indicate a contrary intent.

Thus, in contrast to the position taken by the industry briefs, there is no gap between the requirements for placing a drug on the market in the first instance and those for keeping it there.[28] If there is insufficient data to put the drug on the market, there would be insufficient data to keep an established drug on the market; and if new information showed that the data on which the drug was originally approved for marketing is now regarded as insufficient, the drug must be removed.

The very purpose of the 1962 Amendments requires this result, not only as to the ultimate burden of proof but also with regard to the burden of coming forward. As we have shown, Congress intended to require pre-1962 NDA'd drugs to meet the new effectiveness requirements, after a two-year moratorium during

[28] *Bell* v. *Goddard*, 366 F. 2d 177 (C.A. 7), contains an offhand statement to the contrary, but the question was not in issue in the case and was not briefed or argued to the court.

which the necessary data could be obtained.[29] The drugs had never before been reviewed and approved for effectiveness (if they had been, and the Commissioner's proposed withdrawal of approval was based on specific new evidence or analysis which had come to light, there might be a greater burden upon him to set forth this information in the notice proposing withdrawal of approval). The suggestion that the Commissioner must shoulder the burden of coming forward with a detailed review of the information in his file (and perhaps everything in the medical literature) showing that acceptable evidence of a drug's effectiveness does not exist thus ignores the concrete realities of the situation and the nature of the inquiry the statute requires him to make. It would place upon him the onerous burden of demonstrating a negative—the absence of studies—despite the fact that, if such studies do exist, information regarding them is surely in the manufacturer's files. Neither common sense nor considerations of fairness prevent placing the burden

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[29] The construction urged by the industry briefs would frustrate this intent by placing a much greater impediment to FDA's application of the Amendments to these drugs than to newly marketed therapeutic entities. The situation is virtually identical to that presented in *Environmental Defense Fund v. Finch*, 428 F. 2d 1083 (C.A.D.C.), which involved another section of the Act (relating to pesticides). The court there stated (428 F. 2d at 1092, n. 27):

"In light of Congress' strong concern about the safety of pesticide residues and the congressional intent to place the burden of persuasion on those proposing to permit a residue to remain, the fact that the present petition seeks revocation of an existing tolerance does not affect the burden of persuasion established by Congress. * * * Once new evidence bearing on the safety of pesticide residues has been adduced or cited suf-

of coming forward upon the person best situated to meet it—the manufacturer.[30]

Even if it were concluded that some basis must exist to trigger the imposition on the manufacturer of the burden of coming forward with a concrete showing that substantial evidence of effectiveness may exist, surely this requirement is satisfied by the fact that the National Academy of Sciences, drawing upon the best scientific talent available in the Nation, has concluded that the drug's effectiveness is not established.

C. THE USE OF HISTORICAL CONTROLS FOR EVALUATION OF LUTREXIN IS UNJUSTIFIED, AND THE "CONTROLS" IN HYNSON'S "STUDIES" WERE INADEQUATE ON THEIR FACE

Although Hynson argues that the testimonials presented on behalf of Lutrexin are sufficient in themselves to justify a hearing (Br. 20), ultimately its position rests upon the contention that the use of historical controls in the Gratton and Majewski studies affords sufficient grounds for a hearing (Br.

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ficient to justify reopening the issue of the validity of existing tolerances, as in the present case, the burden of establishing the safety of any tolerance remains on those who seek to permit a residue. In this connection, we note that the statute itself explicitly requires that the procedures for amending or repealing tolerances should be the same as those for establishing tolerances. 21 U.S.C. § 346a(m)."

[30] Since the NAS-NRC panels concluded that more than 13,000 of the claims they reviewed were not supported by substantial evidence (see our brief in *Bentex* at p. 18), FDA would be faced with a truly monumental task if it had to prepare a detailed substantiation of each of these conclusions before it could move against the drug. By placing the burden of coming forward on the manufacturer, the process of weeding out wholly unsubstantiated drug efficacy claims is rendered at least partially manageable.

21-24). The gist of Hynson's position is that it would be unethical to test Lutrexin against a placebo because it is "clinically-proven to be effective" (Br. 20, J.A. 37)—an assertion that assumes the answer to the very question in issue.[31]

It is well recognized that the use of so-called "historical controls," by which a patient or group of patients is compared with the generally expected clinical outcome, is almost as suspect scientifically as the use of clinical impression. Indeed, this procedure is really a simple extension of the concept of clinical impression, because it cannot eliminate the observer's or the patient's bias (*i.e.*, it is not a "blind" study), there is no randomization of subjects, and there is no pairing of controls. Of all types of scientific studies, therefore, it is the most suspect and the least reliable; it is permissible only in rare circumstances.

Professor Walter Modell, one of the nation's foremost pharmacologists, has described the fallacies of the historical control:

> It is tempting to use an easy way out, to use what has been called the historical control, i.e., a recounting of previous or personal experience or recorded experience as a basis of comparison. Often, this is not recognized as a control—and with good reason, for it is a treacherous control.

[31] Lutrexin is claimed to be effective in treatment of dysmenorrhea as well as threatened and habitual abortion. Dr. Rezek claims to have found the drug effective in his practice (J.A. 118-120). No control group was employed. The sole criterion for gauging efficacy was the subjective responses of the patients. Hynson does not contend that dsymenorrhea is either life threatening or predictable in its onset or pattern.

> No method of drug examination is more likely to lead to erroneous conclusions, because it has none of the safeguards provided by other controls, the elimination of placebo effects and of bias. It also fails utterly to provide comparable bases for examinations of control and experimental groups. Only in the case of the disease in which an irrevocable or unquestionable characteristic course has been established, and particularly when the disease is rare, is the historical control justified. [Modell & Houde, *Factors Influencing Clinical Evaluation of Drugs with Special References to the Double Blind Technique,* 167 J. Am. Med. Assn. 2190, 2194 (1958).]

For these very reasons, the FDA regulations require the use of concurrent controls on randomized patients using the double-blind technique, except in rare circumstances where to do so would be unethical. 21 C.F.R. 130.12(a)(5)(ii)(*a*)(*4*)(*iv*) (J.A. 488). Such rare circumstances include acute leukemia, poisonous snake bites, and other similar circumstances where mortality is foreordained.

The use of historical controls in evaluating Lutrexin is not justified, either ethically or scientifically.[32] In

[32] The importance of adequate scientific studies in treating threatened and habitual abortion has recently been dramatically but tragically demonstrated. It was common, during the 1950's, to treat this condition with large doses of the artificial hormone, diethylstilbestrol (DES). When controlled clinical studies failed to show the effectiveness of this drug for that use, however, its use was no longer recommended. Recently, moreover, it has been discovered that this use of DES has been associated with a very rare form of cancer of the vagina in the female offspring of mothers on whom the drug was used. Herbst et al., *Adenocarci-*

numerous other cases involving threatened and habitual abortion, studies have been undertaken with concurrent controls, using the concurrent randomized double-blind technique also required by the FDA regulations.[33] The diagnosis and clinical course of threatened and habitual abortion is highly variable, depending upon the physician, the patient and the clinical conditions.[34] Particularly because of the use of the drug during pregnancy—unquestionably the most dangerous period for drug use—it would be highly unethical

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noma of the Vagina, 284 N. Eng. J. Med. 878 (April 22, 1971); Greenwald et al., *Vaginal Cancer After Maternal Treatment with Synthetic Estrogens*, 285 N. Eng. J. Med. 390 (August 12, 1971). If it had first been required that this drug be studied under controlled clinical conditions, its use for a purpose for which it was ineffective would not have occurred, and the nation would have been spared this tragedy.

[33] Compare the detailed published plan and double-blind technique used in evaluating diethylstilbestrol for this same condition, Himsworth, *The Use of Hormones in the Management of Pregnancy in Diabetics*, 2 Lancet 833 (1955), and Dieckmann, *Does the Administration of Diethylstilbestrol during Pregnancy Have Therapeutic Value?*, 66 Am. J. Ob. Gyn. 1062 (1953), with the unplanned, uncontrolled observations of Gratton (J.A. 87–91) and Majewski (J.A. 92–117) on Lutrexin. Ten copies of the Himsworth and Dieckmann studies are being lodged with the Court for comparison purposes.

[34] For example, Dr. Gratton's "historical controls" show a live birth rate of 46 percent (J.A. 88), whereas the control group in Himsworth, *supra*, shows a fetal survival rate of 75 percent. Dr. Allen, upon whom Hynson relies, has recognized the uncertainty of ascribing benefit to a drug administered in treatment of threatened abortion: "It is, of course, difficult to prove statistically that hormone therapy does save the pregnancy as there are many pregnancies in which bleeding and cramping occur yet the pregnancy proceeds normally with no therapy other than rest in bed" (J.A. 122.).

to permit use without adequate assurance of its effectiveness. If there were adequate alternative drugs for this condition, the only ethical question would be whether Lutrexin could properly be used at all (moreover, the effective drug could properly serve as the positive control); and if there are no adequate alternative drugs, the use of a double-blind study in this situation presents no ethical issues. It is in no way comparable to the virtually certain outcome of such conditions as acute leukemia of childhood.

Even assuming, *arguendo*, that the use of proper historical controls might be justified, no attempt has in fact been made at any stage in this proceeding to justify the adequacy of the controls used by Gratton and Majewski—not even in the brief filed in this Court is it suggested that these historical controls were adequate. The regulations require, for example, that a historical control must show "the adequately documented natural history of the disease and condition in comparable patients or populations." Hynson neither documented the natural history of the disease nor demonstrated that the patients were comparable with respect to such variables as age, medical complications (*e.g.*, Rh factor, trauma, malnutrition, diabetes, and hypertension), use of alcohol and cigarettes, medical treatment during pregnancy (*e.g.*, diet, bed rest, and medication), history of previous pregnancy (*e.g.*, number, type, and history of deliveries, abortions, and miscarriages), and family obstetrical history (*e.g.*, congenital abnormalities). To this day, FDA has been provided with no information sufficient

to justify the assertion that the studies qualify as adequate and well controlled.

Finally, the use of numerous concurrent medications, the lack of a plan or protocol, the lack of any uniform criterion for patient selection, the lack of any uniform definition of "threatened abortion," and the lack of an adequate statistical analysis to show that the results were not due to chance, place these studies wholly outside the requirements of the law and the regulations. Upon close analysis of the Gratton data, it is clear that they are nothing more than a collection of case histories over a ten-year period of private medical practice, and not at all the type of scientific study contemplated by the statute and regulations. In essence, Hynson merely asserts that, at a hearing, it hopes in some way to adduce sufficient testimony to justify the scientific basis for these studies, but it has consistently declined to present any information whatever on the above points to FDA throughout these proceedings.

D. THE LACK OF HEARINGS TO DATE IS NOT SIGNIFICANT

The industry briefs note that FDA has granted no hearings since the agency instituted its summary judgment rule; they argue that this demonstrates the unfairness of the procedure.[35] There are, however, a number of reasons why no manufacturer to date has been able to demonstrate a genuine issue of fact that would justify a hearing.

FDA has implemented the 1962 Amendments by

[35] Hynson Br., No. 72-394, pp. 34-35; PMA Br. 23.

beginning with those drugs regarded as least likely to be effective or as possibly hazardous. A number of these actions have involved antibiotic combinations, which have been in substantial medical disrepute since before the 1962 Amendments, and indeed were the subject of substantial adverse comment during the hearings on those Amendments.[36] Others removed from the market have had shotgun formulas for which no scientific rationale could be imagined.[37] In general, the drugs removed thus far have been trivial at best, have had not the slightest scientific evidence to support them, and were therapeutically obsolete items that should have been discarded many years ago.[38]

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[36] *E.g., Upjohn Co.* v. *Finch*, *supra*; *Pfizer* v. *Richardson*, *supra*; *Hearings on the Drug Industry Antitrust Act before the Senate Subcommittee on Antitrust and Monopoly of the Senate Judiciary Committee*. Pt. 24, 86th Cong., 2d Sess., at 13924–13928.

[37] *E.g., American Cyanamid Co.* v. *Richardson*, 456 F. 2d 509 (C.A. 1); *Bristol Laboratories* v. *Richardson*, 456 F. 2d 563 (C.A. 1).

[38] See, *e.g.*, the detailed analyses contained in recent FDA orders denying hearings in 38 Fed. Reg. 6215–6222, 6296–6309, 6419–6422. The contention in the PMA brief (p. 23, n. 21) that FDA has in one of those orders rejected seven affidavits concluding that studies were adequate and well-controled is misleading. Affidavits were first submitted in support of the contention that adequate and well-controlled clinical studies should not be required for the drug. As an afterthought, when it became clear that such studies were required, affidavits were submitted contending that two studies which, on their face, did not meet the requirements of the statute and regulations, should nevertheless be accepted as adequate and well-controlled. 38 Fed. Reg. 6305, 6307–6308. This is thus an illustration of the industry contention that affidavits must be accepted as true, regardless of whether they are supported by the data submitted (PMA Br. 4).

Drugs on which closer issues are presented may well be forthcoming in the near future. For example, there are many "possibly effective" and "probably effective" drugs on which adequate and well-controlled clinical studies are now in progress.[39]

It is not difficult to foresee issues on which a hearing will be justified. Where FDA believes that the data are fraudulent, for example, and the company disputes that contention, a hearing would obviously be required.[40] Similarly, where the drug is admittedly effective, but there is a question of the benefit-risk ratio (*i.e.*, the drug is regarded as unsafe because its admitted effectiveness is outweighed by its lack of safety), a hearing would ordinarily be required unless there is no rational basis advanced by the manufacturer to support a contrary conclusion. Finally, where the sole issue is effectiveness, and at least two adequate and well-controlled clinical studies are submitted, a hearing might be required if FDA nevertheless rejected either or both as insufficient to demonstrate the effectiveness of the drug.[41]

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[39] Some 56 drugs that were originally classified as "probably effective" or "possibly effective" have since been reclassified as effective by FDA on the basis of new information, without the necessity for a hearing.

[40] This was the situation which resulted in the hearing held on withdrawal of the NDA approval involved in *Unimed, Inc.* v. *Richardson*, 458 F. 2d 787 (C.A.D.C.).

[41] FDA has long required more than one adequate and well-controlled clinical trial, in order to show that the results are

The cases thus far have presented none of these difficult judgmental issues. As the Sixth Circuit said in *Upjohn Co.* v. *Finch*, 422 F. 2d 944, 955, "We agree with the Commissioner that: 'No amount of examination and cross-examination can change the scientific studies and data reported into something they are not.'" When questions are presented on which examination and cross-examination can elucidate differences in judgment, however, FDA clearly anticipates holding hearings on such issues.

E. THE COMMISSIONER'S CONGRESSIONALLY ASSIGNED ROLE AS REGULATOR DOES NOT DEPRIVE HIM OF AUTHORITY TO DECIDE WHETHER A HEARING IS REQUIRED

The industry briefs raise the question whether the Commissioner of Food and Drugs may properly sit in judgment on a summary judgment motion when he is also the moving party on the issue.[42] The Act itself requires the Secretary, who has delegated his authority to the Commissioner, to determine the safety

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reproducible and not due to chance. See 21 C.F.R. 130.4(e), para. 12(c):

"* * * Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. * * *"

The material submitted by Hynson also fails on its face to satisfy this requirement, since, although there is more than one "study," there are not two by independent investigators studying the same use for the drug.

[42] Hynson Br., No. 72-394, pp. 27-30; PMA Br. 13-14.

and effectiveness of new drugs. The industry does not argue that this statutory scheme is unconstitutional, and it well settled that administrative agencies which initiate complaints may also rule upon them.[43]

The Commissioner is no more an advocate and no less an independent arbiter in ruling upon the summary judgment issue than he is in ruling upon the withdrawal issue after a full adjudicatory hearing. *Upjohn Co.* v. *Finch, supra,* 422 F. 2d at 956. The industry cites no case, nor is the government aware of one, which has held that a summary judgment motion stands on any different footing than disposition on the merits after a full hearing. Court review will in both instances reveal whether the Commissioner was arbitrary or capricious and whether there was substantial evidence of record and a basis in law to support his actions.

The Commissioner, unlike some regulatory agencies, has an affirmative duty to promote the marketing of safe and effective therapeutic agents that will help foster the nation's health, as well as the more negative duty to remove unsafe or ineffective drugs from the market. In a true sense, therefore, the Commissioner stands as an independent arbiter on issues of drug safety and effectiveness, applying the impartial and objective standards laid down by the statute and regulations, and not as an advocate for any position.

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[43] *F.T.C.* v. *Cement Institute*, 333 U.S. 683, 701–703.

III. The Scope of the Section 107(c)(4) Exemption

The industry briefs argue that, under the transition provisions contained in Section 107(c)(4) of the 1962 Amendments, only those drugs for which an NDA became effective between 1938 and 1962, and which still remain on the market at this time, are subject to the effectiveness requirements of the Amendments.[44] Some of these briefs would further narrow this coverage of the 1962 Amendments to those drugs within this class for which the manufacturer had not withdrawn the NDA, or to those which were not generally recognized as safe on the day prior to the Amendments. The industry briefs are unanimous in contending that no me-too drugs are covered by the 1962 Amendments.

The net effect of this argument would be to exempt roughly 90 percent of current prescription drugs and over 99 percent of current OTC drugs from the effectiveness requirements of the 1962 Amendments. In short, instead of making the requirement of effectiveness the rule, the industry briefs make it the rare exception. Surely, if Congress had intended this result the legislative history would reflect it.

The government's interpretation of the transition provisions, by contrast, accords to this exemption the result that one ordinarily expects from this type of statutory provision. Interpreting the term "drug" in Section 107(c)(4) to apply generically, as we suggest, would result in coverage by the 1962 Amendments of roughly 95 percent of all current prescrip-

[44] PA Br. 50–64; PMA Br. 41–54.

tion drugs and the majority but not all OTC drugs. Such prescription drugs as digitalis and quinine, and such OTC drugs as aspirin and epsom salts, would fall within the exemption, but these would be the exception rather than the rule.

IV. The Scope of the Section 201(P) Exemption

The industry briefs argue that general recognition of safety and effectiveness presents a wholly different standard from the type of evidence necessary to prove safety and effectiveness under Section 505,[45] and thus that there exists a "double standard" for drugs in the marketplace to which the effectiveness requirement applies. For some, the public can be assured of the product's safety and effectiveness. For others, the public can be assured only that there are some persons who believe them to be safe and effective, although no scientific data exist to back up that belief. The industry briefs do not propose that the products be separately labeled or identified in a way that would enable consumers to determine those which are proved to be safe and effective and those that are only believed without scientific support to be safe and effective.[46]

The implausibility of this position seems apparent on its face. Nothing in the legislative history suggests that Congress intended there to be two classes of drugs covered by the effectiveness requirements.

[45] Bentex Br. 6–7; PMA Br. 32–34.

[46] If this "double standard" in fact existed, FDA would be obligated under Sections 403(a) and 201(n) of the Act to require prominent labeling to distinguish between the two.

Indeed, Congress explicitly rejected clinical impressions and unsubstantiated opinion as a basis for determining safety and effectiveness and demanded adequate scientific proof. If this congressional judgment is to be effectuated, it is clear that there can be no general recognition of safety and effectiveness within the meaning of the Act without adequate scientific evidence to support it.[47]

CONCLUSION

For the foregoing reasons, the judgments in *Bentex* and *Hynson* should be reversed, the judgment in *CIBA* should be affirmed, and the judgment in *USV* should be affirmed on the grounds specified in the government's brief.

Respectfully submitted.

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APRIL 1973.

[47] See, for example, the definitions of "safety" and "effectiveness" promulgated by FDA for OTC drugs, 37 Fed. Reg. 9464, 9474, which require adequate scientific evidence before general recognition of safety or effectiveness may occur.

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